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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/020,721 | 12/14/2001 | Motonao Nakao | HIRA.0054 | 9615 |

7590 10/01/2003

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EXAMINER

CHUNDURU, SURYAPRABHA

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1637 | 13 |

DATE MAILED: 10/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|----------------------|--------------|--|
| Office Action Summary | Application N . | Applicant(s) | |
| | 10/020,721 | NAKAO ET AL. | |
| | Examiner | Art Unit | |
| | Suryaprabha Chunduru | 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2, 4-6 is/are pending in the application.
- 4a) Of the above claim(s) 5 and 6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2, 4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Acknowledgement is made for the request to establish continued prosecution application (RCE) (Paper NO. 11) filed on July 2, 2003. The request for RCE is accepted and is established with the status of the application as follows:

- a. the filling date of this RCE is established as 12/14/2001;
- b. Claims 1 and 3 are canceled. Claims 2, 4-6 are pending. Claims 2 and 4 are considered for examination. Non-elected claims 5 and 6 are withdrawn from further consideration.

2. Applicants' response to the earlier office action (Paper No. 12) filed on July 2, 2003 is reconsidered and has been entered.

Response to Arguments

3. Applicant's response to the office action (Paper No.12) is fully considered and found persuasive in view of arguments.
4. With reference to the rejection made in the previous office action under 35 USC 112 second paragraph, the rejection is withdrawn in view of Applicants' arguments and amendment (Paper No.12).
5. With reference to the rejection maintained in the previous office action under 35 USC 102(b), the rejection is withdrawn in view of cancellation of claims 1 and 3 by the amendment. However Applicant's arguments with respect to claims 1-4 have been considered and found not persuasive. Applicants' particular arguments regarding detection step comprising "entering a fluorescent material in said PCR-amplified base sequences is found not persuasive because excitation of light emitted by a fluorescent material in a broad sense comprises incorporation of labeled nucleotides (such as biotin labeled or fluorescent energy-transfer

labeled) intercalating dyes like ethidium bromide, or cyber green. Further the instant claims do not recite the type of fluorescence material used in the reaction. That is, whether the fluorescent reagent is an intercalating dye like ethidium bromide or cyber green. Thus the rejection is maintained herein with regard to claims 2 and 4 and is re-written herein as below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Schollien et al. (Clin Chem., Vol. 43, No. 1, pp. 18-23, 1997).

Schollien et al. teach a method of instant claim 2, of detecting PCR-amplified base sequences wherein Schollien et al. disclose that the method comprises (i) conducting PCR amplification by mixing a plurality of pairs of primers with a sample (see page 19, column 1, paragraph 3), said primers being suitable for amplifying different base sequences of a same or different lengths by PCR (see page 19, Table 1, see fragment lengths); (ii) conducting a hybridization reaction by using a substrate on which one primer (RBD primer used as a PCR primer) of each said PCR primer pairs are fixed, and a hybridization solution containing said PCR amplified sequences (see page 19, column 1, paragraph 3, column 2, paragraph 1); detecting the hybridization spot on the substrate in which hybridization reaction occurred by processing the entry of the fluorescent material using chemiluminescent kit (see page 19, column 2, paragraph 1). Schollien et al. also disclose the oligonucleotides on the substrate are equivalent to the PCR primers used in the amplification (see page 20, paragraph 1, column 2, paragraphs 1-

4). With regard to the instant claim 4, Schollien et al. teach that the said PCR primers comprise a base length number ranging from 10-30 (see page 19, table 1, page 20, table 2). Thus the disclosure of Schollien et al. meets the limitations in the instant claims.

6. With reference to the rejection made in the previous office action under 35 USC 103(a), Applicant's arguments with respect to claims 1-4 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejection is based on an intercalating agent used as a fluorescent material for detection process.

A. Claims 2 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pastinen et al. (Genome Res., Vol. 7(6), pp. 606-614, 1997) in view Hawkins (USPN. 6,589,778).

Schollien et al. teach a method of instant claim 2, of detecting PCR-amplified base sequences wherein Schollien et al. disclose that the method comprises (i) conducting PCR amplification by mixing a plurality of pairs of primers with a sample (see page 19, column 1, paragraph 3), said primers being suitable for amplifying different base sequences of a same or different lengths by PCR (see page 19, Table 1, see fragment lengths); (ii) conducting a hybridization reaction by using a substrate on which one primer (RBD primer used as a PCR primer) of each said PCR primer pairs are fixed, and a hybridization solution containing said PCR amplified sequences (see page 19, column 1, paragraph 3, column 2, paragraph 1); detecting the hybridization spot on the substrate in which hybridization reaction occurred by processing the entry of the fluorescent material using chemiluminescent kit (see page 19, column 2, paragraph 1). Schollien et al. also disclose the oligonucleotides on the substrate are equivalent to the PCR primers used in the amplification (see page 20, paragraph 1, column 2, paragraphs 1-4). With regard to the instant claim 4, Schollien et al. teach that the said PCR primers comprise a base length number ranging from 10-30 (see page 19, table 1, page 20, table 2). Although Schollien et al. teach a fluorescent reagent for detection Schollien et al. did not teach an intercalating agent as a fluorescent material.

Hawkins teach a method of claim 2 of detecting a target nucleic acid comprising a detecting at least one of the spots on said substrate (biochip) in which the hybridization reaction occurs, by processing a fluorescent material to enter in said target molecules comprising double-

stranded DNA and detecting fluorescence by exciting said fluorescent material contained in said at least one of the spots on the substrate (biochip) (see column 10, lines 64-67, column 11, lines 1-8).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of detecting PCR-amplified base sequences as taught by Schollien et al. with the teachings as taught by Hawkins which is applicable to use intercalating dye as a fluorescent material in signal detection process because Hawkins states that 'detection of hybridization signals by fluorescence is preferred using labeled target molecules or by including intercalating dyes in the hybridization fluid (see column 10, lines 64-67). An ordinary practitioner would have been motivated to combine the method of Schollien et al. with the teachings of Hawkins for the advantages of developing a cost-effective method for detecting PCR-amplified base sequences by including the intercalating dye as a fluorescent material in hybridization reaction because such limitation would reduce the use of expensive fluorescent labeling material in the detection of a target nucleic acid molecule.

B. Claims 2 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pastinen et al. (Genome Res., Vol. 7(6), pp. 606-614, 1997) in view of Longiaru et al. (USPN. 5,232,829) and Hawkins (USPN. 6,589,778).

Pastinen et al. teach a method of instant claim 2, of detecting PCR-amplified base sequences (page 608, column 1, Fig. 1) comprising:

(a) conducting PCR amplification by mixing a plurality of primer pairs with a sample, said primers amplify different base sequences (see page 611, column 1, paragraph 1);

(b) conducting a hybridization reaction by using a substrate on which primers are fixed spotted on spots and a solution containing the amplified base sequences from step (a) and performing said hybridization reaction between the primers on the substrate and said PCR-amplified base sequences (see page 607, column 2, paragraph 2, page 611, column 2, paragraph 3);

(c) detecting at least one of the spots on said substrate in which hybridization reaction occurs (see page 609, column 1, paragraph 1, page 610, column 1, Fig. 2), wherein the detecting the spots comprise (i) processing a fluorescent material (fluorescent ddNTPs) to enter in said PCR-amplified base sequences (incorporation of fluorescent nucleotides) and (ii) detecting the fluorescence generated by exciting said fluorescent material contained in at least one of the spots on the substrate (see page 609, column 1, paragraph 1, page 610, Fig. 2). Although Pastinen et al. teach a fluorescent reagent for detection Pastinen et al. did not teach an intercalating agent as a fluorescent material.

Pastinen et al. also teach with reference to the instant claim 4, that the method comprising primer base length range from 10-30 bases (see page 612, table 2). However Pastinen et al. did not specifically teach said PCR primers used as probes in hybridization reaction.

Longiaru et al. teach a method for detection of a microorganism using a format for hybridization capture of PCR amplified DNA on a solid support wherein Longiaru et al. disclose PCR primers themselves could be used as capture probes in hybridization reaction (see column 7, lines 1-20).

Hawkins teach a method of claim 2 of detecting a target nucleic acid comprising a detecting at least one of the spots on said substrate (biochip) in which the hybridization reaction

occurs, by processing a fluorescent material to enter in said target material comprising double-stranded DNA and detecting fluorescence by exciting said fluorescent material contained in said at least one of the spots on the substrate (see column 10, lines 64-67, column 11, lines 1-8).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of detecting PCR-amplified base sequences as taught by Pastinen et al. with the teachings as taught by Longiaru et al. which is applicable to use PCR primers as probes because Longiaru et al. states that 'capture probes are defined herein as sequences of amplicon within the boundaries of the primers, the primers themselves or oligonucleotides containing primer sequences, may be used as capture probes' (see column 7, lines 12-20). Further combination of Hawkins which is applicable to use intercalating dye as a fluorescent material in signal detection process because Hawkins states that 'detection of hybridization signals by fluorescence is preferred using labeled target molecules or by including intercalating dyes in the hybridization fluid (see column 10, lines 64-67). An ordinary practitioner would have been motivated to combine the method of Pastinen et al. with the teachings of Longiaru et al. and Hawkins for the advantages of developing a sensitive method for detecting PCR-amplified base sequences by including the PCR primers as capture probes in hybridization reaction and intercalating fluorescent dye because such limitations would enhance the detection of PCR-amplified base sequences reduce the use of expensive fluorescent labeling material in detecting a target nucleic acid molecule.

Conclusion


No claims are allowable.

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Suryaprabha Chunduru
September 25, 2003


JEFFREY FREDMAN
PRIMARY EXAMINER